UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/614,037	07/08/2003	Manfred Reiter	14693-0195	9074

61263 7590 02/08/2007

PROSKAUER ROSE LLP
1001 PENNSYLVANIA AVE, N.W.,
SUITE 400 SOUTH
WASHINGTON, DC 20004

EXAMINER	
VOGEL, NANCY S	
ART UNIT	**PAPER NUMBER**
1636	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/614,037	REITER ET AL.	
	Examiner	Art Unit	
	Nancy T. Vogel	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *36-38 and 46-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36-38 and 46-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 34-36 and 46-48 are pending in the case.

Any rejection of record in the previous action not addressed in this office action is withdrawn.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/8/07 has been entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 34-36, 46-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification as originally filed does not provide support for the invention as now claimed: "purified soy hydrolysate at a concentration of about 0.05% (w/v) to less than about 1% (w/v). This a new matter rejection. The specification does not provide sufficient blazemarks nor direction for the instant methods encompassing the above-mentioned limitations, as currently recited. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112. The portions of the specification pointed to by applicant's in their arguments filed 1/8/07, i.e. page 3 [013] and page 9 [31] do not contain the range of concentration of soy hydrolysate currently recited in the claim 34, i.e. "about 0.05% (w/v) to less than about 1% (w/v)". Therefore, the amendment to the claim 34 constitutes new matter.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 34-36 and 46-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 34 and by dependence claims 35, 36 and 46-48, are vague and indefinite in the recitation of "0.05% (w/v)" , "1% (w/v)", "0.3% (w/v)". It is not clear what is intended by these terms. It is not clear whether for example, a solution made from 1

gram of hydrolysate, in 1 liter (1000 ml) of liquid (water or buffer) is intended to be a 0.1% solution, or whether it is intended to be something else. Applicants have argued at page 5 of their response filed 1/8/07, in response to a separate rejection, that the cited Price reference disclosed the generalized concentration range of 10-1000 mg/liter for plant peptides and 10-8000 mg/liter for yeast extract. Applicants state that these correspond to 1% to 100% and 1% to 800% respectively, and that the examiner has therefore miscalculated this concentration. However, it is maintained that for instance, the concentration of 10mg/L, i.e. 0.01g/L, could be interpreted as being a .001%, not 1%, while 1000 mg/L (i.e. 1 g/L) could be interpreted as being .1%, not 1000%. This calculation is based on the following: 1 gram of material in 1 liter or 1000 mls of liquid, which is assumed to be 1000 grams, is 0.1% of that liter. Therefore, since it is not clear what applicants intended by the recitation of terms such as 0.05% (w/v), it is unclear what the intended metes and bounds of the claim are.

Claim 34 and by dependence claims 35, 36, and 46-48 are vague and indefinite in the recitation of "purified soy hydrolysate" since it is not clear what is considered to be encompassed by this phrase. Since the soy hydrolysate is an enzymatic digest of soybean cells comprising numerous undefined components, it is not clear what is intended to be included in a "purified" extract or hydrolysate. Therefore, it cannot be accurately determined what the intended metes and bounds of the claims are.

Claim Rejections - 35 USC § 103

Claims 36-38 and 46-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shibuya et al. (US Patent 6,406,909) (newly cited) in view of Kistner et al. (5,753,489) and Quest International Product Information, Norwich, NY, 1995 and . Sheffield Pharma, (newly cited).

Shibuya et al. disclose a method of culturing animal cells using serum-free medium or components from animals, using soybean protein hydrolysate at 1-5 g per liter, and yeast extract at 1-5 g per liter (col. 2 lines 56-65). The reference discloses that animal cells may be mammalian cells such as CHO, HeLa, BHK, myeloma (col 4 lines 42-48). The reference discloses (col. 8, lines 14-22) the soy hydrolysate may be Hysoy, which is the same as that disclosed in the instant specification at page 9 [30]. The yeast hydrolysate may be Hy-yest, as is disclosed in the instant specification. The reference discloses that this method of culturing cells using animal protein free medium comprising soy hydrolysate and yeast hydrolysate is advantageous since the cells have increased cultivation efficiency, i.e. higher growth rate and higher rate of production or a recombinant protein or peptide (col. 7 lines 45-55).

The difference between the reference and the instant claims is that the cell culture method has the additional steps of infecting the cells with a virus, incubating the cells to propagate the virus, and harvesting the virus or virus antigen produced. . Furthermore, particular sizes of the molecules in the hydrolysates, i.e. 90% of the molecules in the hydrolysates have a molecule weight of less than or equal to 1000 Daltons, is not disclosed.

However, Kistner et al. disclose a method of producing an immunogenic composition comprising virus or virus antigen, comprising providing a culture of a mammalian cells, infecting the cells with a virus, incubating the culture of cells to propagate the virus, harvesting the virus or antigen, and preparing an immunogenic composition from the virus or antigen (see col. 5-6). The virus may be orthomyxoviridae, paramyxoviridae and reoviridae, and the cells may be vertebrate cells such as VERO, CV-1, LLC-MK2, MDCK, MDBK cells (col. 6, lines 1-15). Quest International Product Information discloses that HY-SOY, which is a well known soy hydrolysate, has 25.4% of molecules less than 200 D, 57.5% in the 200-500 D range, and 16.8% in the 500-1000 D range. The product pages disclose that the hydrolysates are useful for applications that require high solubility, including microbiological laboratories and in fermentation products requiring a water soluble, vegetable source peptone.. . Furthermore, technical literature from Sheffield Pharma, current makers of such products as "Hy-Soy"™ and "Hy-Yest" ™ also show that the molecular weight distribution of virtually all products is: 90% of molecules are less than 1 kD in size.

It would have been obvious to one of ordinary skill in the art to have included the steps of infecting the cultured cells with a virus of interest, cultivating the infected cells, harvesting the virus, and isolating an immunogenic antigen therefore, as disclosed by Kistner et al., in the method of culturing animal cells disclosed by Shibuya et al., since both references disclose the growth of cells in culture for the purpose of producing virus or recombinant products of interest. . It would have been further obvious to use well known soy or yeast hydrolysates commercially available, such as those disclosed in the

Quest International Product Information pages, which are disclosed to be "refined" and to have a molecule weight distribution in which at least 90% of the molecules have a molecule weight of less than or equal to 1000 Daltons. Furthermore, technical literature from Sheffield Pharma, current makers of such products as "Hy-Soy"™ and "Hy-Yest" ™ also show that the molecular weight distribution of virtually all products is: 90% of products are less than 1 kD in size. One would have been motivated to do so by the disclosure of Shibuya et al. that the method avoids contamination by animal proteins, and results in increased cultivation efficiency, and the disclosure of the Quest International product information, which discloses that the hydrolysates are refined and are of low molecular weight, and are useful for applications that require high solubility, including microbiological laboratories and in fermentation products requiring a water soluble, vegetable source peptone.. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claims 34-36 and 46-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Price et al. (WO 98/15614) (cited by applicants)in view of Kistner et al. (US Patent 5,753,489) and Quest International Product Information, Norwich NY, 1995, and Sheffield Pharma Ingredients, Cell Nutrition, Hydrolyzed Proteins & Yeast Extracts, Technical Manual, (newly cited).

Price et al. disclose a method of culturing cells comprising providing a culture of cells that have been grown in an animal protein free medium comprising soy

hydrolysate at a concentration of about .1% and yeast hydrolysate at a concentration of0.1% to about .8% (pages 19-20). Price et al. disclose this method is useful for culture of animal cells including human cells and kidney cells (see page 24). Price disclose the method may be used to grow and produce viruses using cell culture (page 2).

The difference between the reference and the instant claims is that the steps of infecting the cells with virus, incubating the infected cells to propagate the virus, harvesting the virus and preparing an immunogenic composition, and specifically, conducting those steps using particular viruses, is not disclosed. Furthermore, particular sizes of the molecules in the hydrolysates, i.e. 90% of the molecules in the hydrolysates have a molecule weight of less than or equal to 1000 Daltons, is not disclosed.

However, Kistner et al. disclose a method of producing an immunogenic composition comprising virus or virus antigen, comprising providing a culture of a mammalian cells, infecting the cells with a virus, incubating the culture of cells to propagate the virus, harvesting the virus or antigen, and preparing an immunogenic composition from the virus or antigen (see col. 5-6). The virus may be orthomyxoviridae, paramyxoviridae and reoviridae, and the cells may be vertebrate cells such as VERO, CV-1, LLC-MK2, MDCK, MDBK cells (col. 6, lines 1-15). Quest International Product Information discloses that HY-SOY, which is a well known soy hydrolysate, has 25.4% of molecules less than 200 D, 57.5% in the 200-500 D range, and 16.8% in the 500-1000 D range. The product pages disclose that the hydrolysates

are useful for applications that require high solubility, including microbiological laboratories and in fermentation products requiring a water soluble, vegetable source peptone.. . Furthermore, technical literature from Sheffield Pharma, current makers of such products as "Hy-Soy"™ and "Hy-Yest" ™ also show that the molecular weight distribution of virtually all products is: 90% of molecules are less than 1 kD in size.

It would have been obvious to one of ordinary skill in the art to have included the steps of infecting the cultured cells with a virus of interest, cultivating the infected cells, harvesting the virus, and isolating an immunogenic antigen therefore, as disclosed by Kistner et al., in the method of cultivating cells disclosed by Price et al., since both references disclose the growth of cells in culture for the purpose of producing virus or recombinant products of interest. It would have been further obvious to use well known soy or yeast hydrolysates commercially available, such as those disclosed in the Quest International Product Information pages, which are disclosed to be "refined" and to have a molecule weight distribution in which at least 90% of the molecules have a molecule weight of less than or equal to 1000 Daltons. Furthermore, technical literature from Sheffield Pharma, current makers of such products as "Hy-Soy"™ and "Hy-Yest" ™ also show that the molecular weight distribution of virtually all products is: 90% of molecules are less than 1 kD in size. One would have been motivated to do so by the disclosure of Price et al. that the method avoids contamination by animal proteins, and the usefulness of the cell culture method for producing virus, and the disclosure of the Quest International product information, which discloses that the hydrolysates are refined and are of low molecular weight, and are useful for applications that require high

solubility, including microbiological laboratories and in fermentation products requiring a water soluble, vegetable source peptone.. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

This rejection is maintained essentially for the reasons made of record in the previous Office action, mailed 9/7/06, plus new reasons as set forth above. Applicant's arguments regarding the previously cited references are addressed below.

Applicants' arguments filed 1/8/07 have been considered but have not been found convincing.

Applicants have argued that "even if Price et al. discloses the term "soy hydrolysate" [sic] does not make the claimed invention obvious when combined with the disclosure of Kistner disclosure" (page 5), and go on to state that the examiner miscalculated the amount of soy and yeast concentration present in the culture medium disclosed by Price et al. Applicants state that Price disclosed the generalized concentration range of 10-1000 mg/liter for plant peptides and 10-8000 mg/liter for yeast extract. Applicants state that these correspond to 1% to 100% and 1% to 800% respectively. However, it is maintained that for instance, the concentration of 10mg/L, i.e. 0.01g/L, would be most likely to be interpreted as being a .001%, while 1000 mg/L (i.e. 1 g/L) would be interpreted as being .1% (i.e. 1 ml of water weighs 1 gram, therefore 1 gram of water per liter (1000 grams or 1000 ml) is .1% of a liter). (It is noted that a new rejection based on the lack of clarity in terms such as "0.05% (w/v)"

has been made.). Furthermore, applicants' arguments that the rice hydrolysate is disclosed as preferred by Price et al., does not obviate the rest of the disclosure, which includes the recitation of soy and yeast extracts. Applicants have argued that the degree of purity currently recited in the claims is not disclosed in the references. The Price reference does not disclose the size of the molecules in the recited hydrolysate. However, according to the Quest International Product Information sheet for Hy-Soy, (1995), which is a well known soy hydrolysate used in the art, the molecular weight distribution is 25.4% less than 200 D, and 57.5% in the 200-500 D range, and 16.8% in the 500-1000 D range. Furthermore, technical literature from Sheffield Pharma, current makers of such products as "Hy-Soy"™ and "Hy-Yest" ™ also show that the molecular weight distribution of virtually all products is 90% less than 1 kD in size. Regarding the term "purity" it is noted that this term is unclear (see rejection under 35 USC 112 p. 2 above), and further, it appears that commercially available and well known hydrolysate are generally regarding as "refined" or "purified". Therefore, it is maintained that the reference is properly cited and the rejection is maintained.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy T. Vogel whose telephone number is (571) 272-0780. The examiner can normally be reached on 6:30 - 3:00, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

NV
1/31/07

NANCY VOGEL
PRIMARY EXAMINER